Gastroesophageal reflux disease and oesophageal cancer

Emer G. N. J. Tytgat
Academic Medical Center, Amsterdam, The Netherlands

During the last decades, the incidence of oesophageal adenocarcinoma has increased almost 400%. Most of those cancers are believed to develop from a precursor lesion, the so called Barrett's oesophagus. Barrett's oesophagus is a condition in which the normal squamous lining of the distal oesophagus has been replaced by columnar epithelium often with intestinal metaplasia. Malignant degeneration of Barrett's oesophagus is thought to be a multi-step process in which intestinal metaplasia progresses through low grade dysplasia and high grade dysplasia into intramucosal and ultimately invasive carcinoma. Endoscopic surveillance, aimed at identifying patients with early and durable malignancy, is currently considered the monitoring technique of choice in patients with Barrett's oesophagus.

Early neoplastic lesions are difficult to identify. In the absence of visible abnormalities, four quadrant biopsies are randomly taken for every two centimetres length of Barrett epithelium.

In the last decade, many new endoscopic techniques have been evaluated for their potential role in improving the accuracy of the detection of early neoplasia. High-resolution endoscopes with high-quality CCD-chips (above 850,000 pixels) and a variable focal distance are now commercially available. High-resolution endoscopy can adequately distinguish areas of intestinal metaplasia from areas with gastric type mucosa. The detection of early neoplasia can be further enhanced by the use of dyes, such as methylene blue and indigo carmine. Methylene blue is a vital stain that is absorbed in areas of intestinal metaplasia. Methylene blue staining is time consuming and operator dependent. Some therefore prefer to combine high-resolution endoscopy with indigo carmine contrast staining.

Narrow band imaging (NBI) is a high-resolution endoscopic technique that aims at enhancing the fine structure of the mucosal surface without the use of dyes. The mucosa is sequentially illuminated with red, green and blue light. The reflected red, green and blue light images are detected by a monochromatic CCD-chip that sends these images to an image-processor that is synchronised with the rotary RGB-band pass filters. Apart from the standard RGB-band pass filters for white light endoscopy, the NBI system has a special set of RGB

Prof. Emer GNJ Tytgat, M.D., Ph.D.,
Chairman EAGE Postgraduate Course Programme
Meibergdreef 9
NL-1105 AZ Amsterdam, The Netherlands
Phone: +31 20 566 3534
E-mail: g.n.tytgat@amc.uva.nl

filters in which the band-pass ranges have been narrowed and the relative contribution of blue light has been increased. NBI improves the recognition of mucosal and vascular patterns in Barrett's oesophagus.

Tissue autofluorescence occurs when tissues are exposed to light of a short wavelength (usually ultraviolet or blue light, as certain endogenous biological substances (fluorophores) are excited causing them to emit fluorescent light of a longer wavelength). Early neoplastic changes cause a different autofluorescent wave pattern than normal tissue.

The incidence of high-grade dysplasia and early cancer in Barrett patients is currently estimated at 0.5% per year and the cost-effectiveness of any surveillance strategy has been questioned. The vast majority of Barrett patients will never develop oesophageal cancer, thus including them in an expensive and labour intensive endoscopy programme using high-tech imaging techniques is even more questionable. Hopes are set, therefore, on the detection of molecular markers to identify those patients that are truly at risk for malignant degeneration.

The standard therapy for high-grade dysplasia and early cancer in Barrett patients has always been radical oesophagectomy. The five year survival rate after surgery in such patients is excellent. The mortality and morbidity of this procedure, however, are 3–5% and 40–50% respectively, even in expert centres. With oesophagectomy, the functional oesophagus is lost which may be associated with a reduced quality of life. Since the risk of lymph node involvement or metastasis to distant sites is small and negligible in such cases, local endoscopic therapy might be a less invasive treatment alternative. Such endoscopic mucosal resection for high-grade dysplasia or mucosal cancer should only be performed after extensive work-up using high-resolution endoscopy, a standard biopsy protocol, expert histopathological evaluation and endoscopic ultrasound. Endoscopic mucosal resection has a low complication rate and preserves the functional oesophagus. Other endoscopic ablation techniques should only be used as an adjunct to mucosal resection. After endoscopic treatment, rigorous follow-up is imperative since the current techniques are still associated with a high recurrence rate. In the future, they will be replaced by techniques that allow radical mucosal resection of the whole Barrett segment.